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HIV-1 IMPACT ON ORAL HEALTH-RELATED QUALITY OF LIFE: A CROSS-SECTIONAL STUDY

David Ribeiro Braz

Dissertação

Mestrado Integrado em Medicina Dentária

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Dissertação orientada pelo Professor Doutor António Mata

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ABBREVIATIONS

ART	Antiretroviral therapy
CI	Confidence interval
DMF	Decayed-missing-filled
DMFt	Decayed-missing-filled teeth
HAART	Highly active antiretroviral therapy
HIV	Human immunodeficiency virus
NGO	Non-governmental organization
OHIP	Oral Health Impact Profile
OHIP-Pt	Portuguese version of the Oral Health Impact Profile
OHRQOL	Oral health-related quality of life
PR	Prevalence Ratio
QOL	Quality of life

ABSTRACT

Objectives: To assess the impact of HIV-1 infection on the OHRQOL in individuals with dental treatment needs using the OHIP-49 and to determine which additional factors contribute to an increase on the social impact of oral conditions among HIV-1 positive patients.

Materials and Methods: This was a cross-sectional analytic study that compared two groups of patients. Group 1 (n=60) consisted of HIV negative patients, group 2 (n=265) consisted of patients from the same socio-economic environment but HIV-1 positive. The proportion of positive impacts in the 49 questions of the OHIP and prevalence ratios between groups were calculated with 95% confidence intervals. OHIP total and subscale scores were determined by addition and presented as mean ± standard error of mean. A stepwise regression analysis was carried out to determine the contributions of the possible explanatory variables on different levels and total OHIP scores. The significance level was set at $\alpha=0.05$.

Results: Cronbach's alpha statistic values obtained for each of the subscales ranged between 0.82 and 0.98, indicating excellent reliability. Patients in group 2 experienced an increased proportion of positive impacts in every question, ranging from 37% to 84% versus 9% to 79% in group 1. Group 2 demonstrated significantly higher ($P<0.05$) OHIP total score (86.16 ± 2.41 vs. 67.32 ± 2.41) and subscale scores, except for "Physical Pain", "Physical Disability" and "Social Disability" subscales. HIV-1 infection presented an independent effect in the reduction of the OHRQOL for total and all subscales of the questionnaire. Variables "DMFt index", "at least one anterior tooth missing" and "drug use" were found to have an independent effect on questionnaire scores.

Conclusions: HIV-1 infection has an independent and negative impact on the OHRQOL. Additional factors like a high DMFt index, prostodontic needs and drug use contribute to a worst OHRQOL of people living with HIV.

Keywords:
HIV-1 infection; dental treatment needs; Oral Health-Related Quality of Live; OHIP-49

RESUMO

Com o aparecimento da terapia antiretroviral (TAR) altamente ativa em meados dos anos 90 e a sua ampla aplicação como tratamento do vírus da imunodeficiência humana (VIH), têm-se verificado aumentos notáveis nas taxas de sobrevivência, bem como uma diminuição da incidência de infeções oportunistas e da Síndrome da Imunodeficiência Adquirida (SIDA), conferindo à infeção pelo VIH o estatuto de doença crónica.

Uma vez que a esperança média de vida dos indivíduos infetados pelo VIH tem vindo a aumentar, o estudo da sua qualidade de vida (QV) emerge como um fator de extrema importância. Os problemas orais que surgem associados à doença podem conduzir a um desconforto físico, funcional e emocional, disfunção ou incapacidade, afetando assim a qualidade de vida relacionada com a saúde oral (QVRSO) destes pacientes.

Ao longo de vários anos, os índices clínicos como o índice de dentes cariados, perdidos e obturados (CPO) têm sido utilizados para medir a saúde oral. No entanto, apesar destes índices refletirem a patofisiologia das doenças orais, não têm em consideração as características multidimensionais das mesmas como o impacto no dia-a-dia dos pacientes. Assim, a necessidade de avaliar a QV na área da medicina dentária levou ao desenvolvimento de vários instrumentos, entre os quais se destaca o questionário *Oral Health Impact Profile* (OHIP). Este questionário foi desenvolvido em 1994 com o objectivo de medir as perceções individuais do impacto associado às condições orais. A versão original do OHIP é constituída por 49 questões que englobam as dimensões física, social e psicológica. Estas encontram-se distribuídas por sete domínios: a limitação funcional, a dor física, o desconforto psicológico, a disfunção física, a disfunção psicológica, a disfunção social e, por último, o *handicap*. A única versão portuguesa consiste numa adaptação para a cultura brasileira, a qual demonstrou ser reprodutível e válida.

Os pacientes infectados pelo VIH apresentam frequentemente uma condição oral precária, com necessidade de intervenção terapêutica profunda a nível da reabilitação oral. Em estudos anteriores, foi observado que as lesões orais associadas à infeção pelo VIH-1 têm um impacto negativo na QVRSO e que este impacto diminui após tratamento dentário. Foi também sugerido que fatores como o género, a afinidade populacional, a existência de cáries dentárias e doença periodontal, o tabagismo, o consumo de cocaína,

a utilização de próteses e não consultar um dentista no último ano estão associados a um impacto psicossocial e funcional. Contudo, o efeito independente da infeção pelo VIH-1 na QVRSO ainda não se encontra esclarecido.

Objetivos: Avaliar o impacto da infeção pelo VIH-1 na QVRSO em indivíduos com necessidades de tratamento dentário, utilizando o questionário OHIP-49. Determinar que fatores adicionais contribuem para um aumento do impacto social das condições orais nestes mesmos pacientes.

Materiais e métodos: Foi realizado um estudo analítico seccional cruzado que comparou dois grupos de pacientes de uma clínica dentária de uma Organização Não Governamental (ONG) portuguesa, com necessidades de tratamento dentário prévias ao início do estudo. O grupo 1 (n=60) integrou pacientes VIH negativos e o grupo 2 (n=265) consistiu em pacientes VIH-1 positivos do mesmo contexto socioeconómico e cultural. Após verificação do cumprimento dos critérios de inclusão e obtenção do consentimento informado, livre e esclarecido, um dos dois investigadores treinados e calibrados realizou a recolha de informação sociodemográfica (género, idade, ocupação profissional e habitação), informação referente a fatores comportamentais (utilização de drogas) e informação clínica (presença ou ausência de coinfecção pelo vírus da hepatite B e C, carga viral, contagem de células CD4+ e realização ou não de TAR). Medições objetivas, tais como o índice CPOD e o *Simple Periodontic Status* (Índice Periodontal Simplificado) por sondagem dos dentes de Ramfjord, bem como uma observação intra-oral completa para estabelecimento das necessidades de tratamento do paciente foram realizadas. Foi administrado a cada paciente o inquérito OHIP-49. Pediu-se aos mesmos para dar, a cada uma das 49 questões, a resposta mais imediata que lhes surgisse em vez daquela que parecesse a mais correta para o investigador. Os pacientes foram também encorajados a pedir ao investigador, sempre que necessário, para repetir a questão ou para explicar algum aspeto relacionado com a mesma que não tivesse sido percebido, antes de fornecerem uma resposta. Se o paciente não fosse capaz de dar uma resposta a 9 ou mais questões do inquérito era imediatamente excluído da análise.

A análise estatística consistiu em estatística descritiva e análise multivariada. Os dois grupos foram comparados relativamente às características clínicas e sociodemográficas utilizando o teste do qui-quadrado de independência ou o teste exato de Fisher para variáveis categóricas e o teste t-Student para variáveis contínuas com um

valor de P bicaudal <0.05 considerado estatisticamente significativo. A consistência interna e fiabilidade dos questionários foram avaliadas através do coeficiente α de Crohnbach, o qual pode apresentar valores entre 0-1, com valores mais elevados a indicar uma maior fiabilidade. Para a análise do OHIP-49, foi realizada, inicialmente, uma contagem de frequências simples, na qual respostas "ocasionalmente", "repetidamente" ou "sempre" foram classificadas como impacto positivo. As percentagens de impacto positivo foram registadas como razão de prevalência para cada questão e analisadas em dois grupos com 95% de intervalo de confiança (IC).

Os *scores* totais e de cada subescala foram determinados por adição, sendo atribuído um valor de 0 a 4 correspondente a cada uma das 5 categorias de resposta ("nunca" – 0; "raramente" – 1; "às vezes" – 2; "repetidamente" – 3; "sempre" – 4). As pontuações obtidas foram apresentadas como Média ± Erro Padrão de Média (EPM). Foi realizada uma análise de regressão *stepwise* para determinar a contribuição das variáveis independentes, com diferenças significativas entre os dois grupos, nas diferentes subescalas e *score* total do OHIP. A partir daí, um modelo linear geral foi utilizado para estimar as médias dos *scores* totais e de cada subescala em ambos os grupos, ajustadas para as variáveis incluídas no modelo e derivadas da regressão previamente realizada. Foram realizadas comparações pareadas entre os dois grupos com correções de Bonferroni e o nível de significância estabelecido em α=0.05.

Resultados: Os valores estatísticos do coeficiente α de Crohnbach para cada uma das 7 subescalas variaram entre 0.82 e 0.98, indicando uma excelente consistência interna do questionário. Os pacientes VIH-1 positivos experienciaram uma proporção mais elevada de impactos para cada uma das questões, variando de 37% a 84% quando comparados com o espectro de 9% a 79% do grupo VIH negativo. Foram observados valores significativamente elevados (P<0.05) no grupo 2 comparativamente com o grupo 1 nas cotações totais do OHIP (86.16 ± 2.41 EPM vs. 67.32 ± 5.67 EPM) e na cotação de cada uma das subescalas, excetuando as categorias "Dor Física", "Disfunção Física" e "Disfunção Social". A infeção pelo VIH-1 apresentou um efeito independente na diminuição da qualidade de vida em todas as subescalas e no *score* total. As variáveis "Índice CPOD", "ausência de pelo menos um dente anterior" e "utilização de drogas" também apresentaram um efeito independente no *score* dos questionários.

Conclusões: Tendo em conta as limitações desde estudo, pode concluir-se que a infeção pelo VIH-1 tem um impacto independente e negativo na QVRSO. Fatores adicionais como um índice CPOD elevado, a existência de necessidades prostodônticas e a utilização de drogas apresentam também uma associação independente com os *scores* do OHIP, tendo assim um efeito negativo na QVRSO destes pacientes.

Na conjuntura atual, devido à fraca saúde oral e à elevada necessidade de tratamentos dentários, esta população representa um grupo prioritário no acesso a estes cuidados. Estudos prospetivos futuros deverão avaliar o efeito da reabilitação oral na qualidade de vida destes indivíduos.

Palavras-chave:
Infeção pelo VIH-1; necessidades de tratamento dentário; Qualidade de Vida Relacionada com a Saúde Oral; OHIP

I. INTRODUCTION

Since it was first recognized in early 1980s, the global pandemic of human immunodeficiency virus (HIV) has caused millions of deaths and has affected the welfare of many more (Giri *et al*., 2013).

In 2013, there were 35 million people living with HIV globally (UNAIDS, 2014). In that same year, Portugal was the country with the third highest population rate of HIV diagnoses of all the European Union member states with a total of 47390 HIV infection cases in different stages of disease (ECDC/WHO, 2014).

With increasing availability of highly active antiretroviral therapy (HAART), fewer deaths have been observed and HIV infection is now regarded as a chronic disease (Boyd, 2009). However, with increases in life expectancy, HIV positive individuals are experiencing more age-related co-morbid conditions, which are affecting their quality of life (QOL) (Justice, 2010).

Oral manifestations are common in people living with HIV and some of them have been recognized as early markers of infection and as predictors of disease progression. Among the most common oral manifestations of HIV are oral candidiasis, oral hairy leukoplakia and necrotizing ulcerative periodontitis (Coogan *et al*., 2005; Ranganathan & Hemalatha, 2006). Changes in the quantity and quality of saliva, usually associated to medication or to the proliferation of CD8+ cells in the major salivary glands can also give rise to rapidly advancing dental decay and loss of teeth (Reznik, 2005). Oral problems may lead to discomfort, dysfunction, or disability which has been shown to affect the overall QOL of HIV positive individuals (Coulter *et al*., 2002; Yengopal & Naidoo, 2008).

For a long time, clinical indices like the decayed-missing-filled (DMF) index have been used to measure oral health. However, these indices fail to take into account multidimensional measures of diseases that consider the patient's perspective and the impact of oral problems on day-to-day life (Corson *et al.*, 1999; Yengopal & Naidoo, 2008). The need to evaluate the QOL in the field of dentistry has led to the development of different oral health-related quality of life (OHRQOL) instruments (Corson *et al.*, 1999), including the Oral Health Impact Profile (OHIP). The questionnaire was developed in 1994 by Slade & Spencer and measures individual perceptions of impact (Slade & Spencer, 1994).

Previous studies (Coates *et al.*, 1996; Yengopal & Naidoo, 2008) have strongly suggested that oral manifestations associated with HIV infection have a negative impact on the OHRQOL and that impact diminish after dental treatment (Marques, 2010). Three other studies (Mulligan *et al.*, 2008; Tomar *et al.*, 2011; Jenganathan *et al.*, 2011) have revealed that factors like gender, race, living situation, dental caries, periodontal disease, smoking status, cocaine consumption, denture use and not consulting a dentist in the previous year were associated with psychosocial and functional impact of oral disorders. However, the independent effect of HIV-1 infection on the OHRQOL remains unclear.

II. OBJECTIVES

The aims of this study were to:

(1) Assess the impact of HIV-1 infection on the OHRQOL in individuals with dental treatment needs using the OHIP-49;

Hypothesis: HIV-1 infection has an independent and negative impact on the OHRQOL.

(2) Determine which additional factors contribute to an increase on the social impact of oral conditions among HIV-1 positive patients;

Hypothesis: Socio-demographic and clinical variables have an independent and negative effect on the OHRQOL.

III. MATERIALS AND METHODS

This study is part of a large scale project taking place in the Oral Biology and Biochemistry Research Group (GIBBO) of the Dental School of the Lisbon University (FMDUL) titled "Host immune factors and periodontal disease in HIV-2 vs. HIV-1 infection". Data collection was performed by Dr. Joana Marques and Dr. Marcos Veiga between January 2010 and January 2015 and posteriorly analysed to reach the aims of this study.

1. STUDY PARTICIPANTS

This was a cross-sectional analytic study that compared one group of HIV-1 positive (n=265) and a control group of HIV negative patients (n=60), recruited consecutively from ABRAÇO, an non-governmental organization (NGO) outpatient clinic, located in Lisbon, which provides full oral rehabilitation for HIV infected people and their relatives.

For inclusion, patients had to be able to communicate in Portuguese, they had to be at least 18 years old at the time of study, HIV positivity had to be confirmed by a laboratory test and signed informed consent had to be provided. Ethical clearance was provided by both Institutional Board reviews at ABRAÇO and Dental School of the Lisbon University.

2. MEASURES

All subjects who participated in this study were invited to answer the Portuguese version of the Oral Health Impact Profile (OHIP-Pt). The instrument was developed from the original OHIP questionnaire (Slade & Spencer, 1994), which is a comprehensive and widely used instrument for assessing the impact of oral health on the QOL.

An extensive body of literature documents its validity and reliability among adults (Slade, 1997, 1998; Allen *et al.*, 2001; Soe *et al*., 2004; Locker *et al*., 2004). The internal consistency and the convergent and discriminative validity of the Portuguese version of the OHIP have been previously reported (Pires *et al*., 2006). In addition, the OHIP has been shown to be reliable (Slade, 1997; Soe *et al*., 2004) and sensitive to changes (Slade, 1998; Allen *et al*., 2001), and to exhibit suitable cross-cultural consistency (Allison *et al*., 1999).

This instrument consists of 49 questions organized into 7 dimensions: Functional Limitation (9 questions), Physical Pain (9 questions), Psychological Discomfort (5 questions), Physical Disability (9 questions), Psychological Disability (6 questions), Social Disability (5 questions), and Handicap (6 questions). Each question had 5 response categories ranging from "never" to "very often". The questions referred to the subject's experience in the previous 12 months. Although item weights were developed for the OHIP, they were not used in the calculations for this study, since Allen *et al.* (Allen *et al.*, 2001) found that the poorest sensitivity to change in QOL was associated with the weightstandardized scores.

3. PROCEDURES

The previously mentioned investigators, trained and calibrated for the clinical methods and diagnostic criteria used by this study, conducted all interviews, clinical examinations, and treatment planning.

Socio-demographic information was obtained for gender, age, employment, and housing, as well as behavioural factors like drug use. A clinical history was gathered for all patients including hepatitis B and C co-infections and for HIV-1 positive patients, viral load data, CD4 counts and presence of antiretroviral therapy (ART) were also obtained. Oral clinical measures included the DMFt index (Klein *et al*., 1938), Simple Periodontic Status obtained by probing Ramfjord teeth and a full mouth observation for the establishment of patient's dental treatment needs.

The 49-item OHIP instrument, comprising 7 subscales, was administered in the form of an interview with each participant using a standardized format. Patients were informed that they would be asked a series of questions for which there was no right or wrong answer. A4-size sheets of paper were then placed in front of them and they were told that each of their responses could be any one of the following: 4-very often; 3-fairly often; 2-occasionally; 1-hardly ever; 0-never. The participants were encouraged to give the answer that immediately came to mind rather than spending time thinking about a response that they felt would be more appropriate, i.e., obsequiousness bias, providing a response that seems more right for the interviewer. Patients were also encouraged to ask the interviewer to repeat the question or explain any aspect of the question that they could not understand before providing an appropriate response where necessary. If patients could not provide a response for more than 9 questions, they were excluded from the analysis.

4. STATISTICAL ANALYSIS

The statistical analysis comprised descriptive statistics and multivariate analyses.

The two groups were compared for equivalence on socio-demographic and clinical characteristics using chi-square test of independence or Fisher's exact test for categorical variables and Student's t test for continuous variables with a two-sided P value <0.05 considered statistically significant.

Internal consistency, reliability of OHIP-49 and corresponding subscales were assessed using Cronbach's formula for coefficient alpha (α) as an estimate of precision, scaled 0–1 with higher values indicating greater reliability (Bland & Altman, 1997).

The primary analyses focused on the estimation of differences between the two groups on the OHIP subscale scores. It was intended to compare the proportion of subjects according to treatment assignment who reported a problem occurring "hardly ever" or "never" vs. "occasionally", "fairly often", or "very often" on each of the OHIP items. A dichotomous variable was created to compare the proportions of subjects in both groups who reported no impact on a particular item, i.e., the problem has no negative influence on their lives, with the proportions reporting some impact. Relative prevalence for positive impact in HIV-1 positive versus control was calculated for each OHIP item with 95% confidence intervals (CI).

For the OHIP evaluations, total and subscale scores were determined by addition. The 5 response categories were assigned values of 0 to 4, and all 49 item values were summed to generate the OHIP-ADD score. Thus, the maximum total score was 196. The maximum subscale scores ranged from 20 to 36 depending on the number of questions within the dimension (see above). Within the OHIP questionnaire, missing values were replaced with the mean for the purposes of the statistical analysis.

Linear multiple regression analysis was carried out to determine the contributions of the possible explanatory variables on different levels and total OHIP scores. A stepwise multivariate regression model was created, interaction was assessed by grouping together a cross-product term with its precedent terms, and decided to enter it into the model on the basis of the significance of the group's joint F test. From there, a general linear model was used for estimation of the means of subscale and total scores in the two groups adjusted for covariates included in the model and derived from the regression previously effectuated. Pairwise comparisons with Bonferroni adjustment were performed between the two groups and significance was set at $\alpha=0.05$.

IV. RESULTS

1. SOCIO-DEMOGRAPHIC VARIABLES

A total of 325 patients (60 group 1 and 265 group 2) were included in this study. 56 patients (92%) in group 1 and 265 (100%) in group 2 completed the questionnaire satisfactorily. In group 1 a number of 3 patients (6%) left more than 9 questions unanswered and 1 patient (2%) told the examiner that the questionnaire was too long and changed opinion about his participation.

Table I highlights the socio-demographic variables and behavioural factors that were assessed and compared in the study groups. Patients were recruited from a population with similar socio-economic indicators. Nevertheless, there was some heterogeneity present between the two groups. The majority of the participants were male, although there were significantly more female (P=0,005) in group 1 (HIV-) compared with group 2. Moreover, group 1 mean age was lower, with increased student proportion and less unemployed or drug users.

Table I. Socio-demographic variables and behavioural factors for the study groups

Item	*Group 1* (HIV-)	*Group2* (HIV+)	*P value*
Sample Size (n)	56	265	
Gender (%)			
Male	36	64	0,005
Female	64	35	0,005
Transgender	0	1	0,317
Age (years)	34,02 +/- 17,4	42,25 +/- 9,7	0,010
Housing (%)			
Owned	25,7	20,6	0,466
Not owned	74,3	79,4	0,354
Employment (%)			
Unemployed	24	49	0,003
Student	28	2	0,000
Employed	34	25	0,241
Retired	14	24	0,105
Drugs (%)			
No	92	41	0,001
Yes	8	59	0,000

2. CLINICAL VARIABLES

Table II provides information on some clinical variables obtained through clinical examination, patient interview, or analysis of data.

Despite DMFt index being elevated in both groups, patients in group 2 produced significantly increased scores when compared with group 1. These differences were expressed in the number of decayed and missing teeth since comparison of filled teeth failed to produce any significant differences. Moreover, HIV-1 positive patients had a significant proportion increase in anterior and posterior teeth missing and in periodontic and prostodontic needs.

Clinical features of HIV-1 infected patients were also recorded for characterization purposes: 80% were on ART, 74% had undetectable viral loads but 45% had CD4 counts under 350. C hepatitis was the more prevalent co-infection affecting 30% of the patients.

Table II. Clinical variables for the study groups

Item	*Group 1* (HIV-)	*Group2* (HIV+)	*P value*
DMFt (mean value)	13,3	21,3	0,000
D	5,9	9,1	0,001
M	6,27	10,91	0,005
F	1,1	1,4	0,625
Periodontic needs (%)	11	22	0,006
Prostodontic needs (%)	51	94	0,007
At least 1 anterior tooth missing	26	50	0,006
At least 1 posterior tooth missing	58	91	0,007
HIV-1 characteristics			
Co infections (%)			
HBV	0	7	
HCV	0	30	
CD4 count (%)			
CD4 >350	100	55	
CD4 <350	0	45	
Viral Load (%)			
Viral load undetectable	100	74	
Viral load detectable	0	26	
Antiretroviral therapy (ART) (%)			
On ART	0	80	

3. OHIP RESULTS

Cronbach's alpha statistic for each subscale was calculated to determine the reliability of the observations recorded for each of the questions within the subscale. A more consistent within-subject response and greater variability between subjects in the sample result in a high alpha score, which ranges between 0 and 1 (values near 0 indicate low reliability and values near 1 indicate high reliability). The values obtained for each of the 7 subscales ranged between 0.82 and 0.98, indicating excellent reliability.

Table III illustrates the differences in the proportion of simple frequency counts of positive impacts in the 49 questions of the OHIP questionnaire between the two groups. Prevalence ratios (PR) and respective 95% CI are also produced for better interpretation.

HIV-1 positive patients experienced an increased proportion of positive impacts in every question, ranging from 37% to 84% versus 9% to 79% in the HIV negative group.

Functional Limitation. Within this subscale higher prevalence rates in HIV-1 positive patients (all PR above 1.8 and with 95% CI with lower limits above 1, which is the line of equivalent prevalence between the two groups) were found for the following questions: "trouble in pronouncing words", "felt that appearance has been affected", "felt that sense of taste has worsened, "felt that digestion has worsened" and "felt that dentures have not been fitting properly".

Physical Pain. Although impact records in this domain were highly prevalent in HIV-1 positive patients, this subgroup of questions produced the lower PR between groups in the questionnaire, with 95% CI lower limits frequently down warding 1 and consequently precluding the significance of the measurements. However, this lack of significance in PR was due to elevated prevalence of impacts in both groups.

Psychological Discomfort. The number of positive impacts was significantly elevated in HIV-1 positive patients for every question within this subscale. Questions where PR was over 2 included "been self-conscious", "been miserable" and "felt tense", with 95% CI between 1.37 and 3.31.

Physical Disability. The questions included in the subscale relate to speech, eating and tasting capabilities, dentures function and comfort. HIV-1 positive patients expressed increased impact proportion in every question when compared with the HIV negative group. PR reflected these differences significantly, with bigger differences in questions "speech has been unclear", "felt there has been less flavour in food" and "had an unsatisfactory diet" whose values were 2.01, 1.91 and 2.36, respectively.

Table III. Comparison of proportions of positive impacts in the 49 questions of the OHIP questionnaire between the two groups and prevalence ratios (PR) (95% CI). Statistically significant results are highlighted in light grey

OHIP question	Group 1 (%)	Group 2 (%)	PR	95% CI
Functional Limitation				
1 Had difficulty chewing any foods	63	76	1,21	1.02-1,51
2 Trouble pronouncing words	25	49	1,95	1,22-3,12
3 Noticed a tooth which doesn't look right	79	84	1,12	1.01-1,3
4 Felt that appearance has been affected	32	76	1,91	1,28-2,85
5 Felt that breath has been stale	53	68	1,30	1,00-1,69
6 Felt that sense of taste has worsened	30	58	1,91	1,27-2,88
7 Had food catching in their teeth or dentures	64	81	1,28	1,04-1,57
8 Felt that digestion has worsened	27	51	1,89	1,21-2,97
9 Felt that dentures have not fitting properly	26	59	2,27	1,12-4,58
Physical Pain				
10 Had painful aching in mouth	55	64	1,15	0,9-1,48
11 Had a sore jaw	46	53	1,17	0,86-1,59
12 Had headaches	38	42	1,11	0,77-1,60
13 Had sensitive teeth with hot or cold food or drinks	64	78	1,22	1,01-1,52
14 Had tooth aches	66	68	1,03	0,84-1,27
15 Had painful gums	55	67	1,21	0,94-1,55
16 Found it uncomfortable to eat any foods	71	81	1,15	1,08-2,59
17 Had sore spots in the mouth	51	58	1,14	0,87-1,52
18 Had uncomfortable dentures	27	66	2,41	1,21-4,83
Psychological Discomfort				
19 Been worried by dental problems	65	82	1,21	1,03-1,56
20 Been self-conscious	33	74	2,25	1,53-3,31
21 Been miserable	30	63	2,08	1,37-3,17
22 Felt uncomfortable about appearance	45	74	1,62	1,20-2,20
23 Felt tense	33	67	2,02	1,37-2,97
Physical Disability				
24 Speech has been unclear	24	48	2,01	1,23-3,29
25 People misunderstood some words	22	39	1,76	1,01-2,97
26 Felt there has been less flavour in food	27	52	1,91	1,22-2,99
27 Been unable to brush teeth properly	39	58	1,49	1,04-2,11
28 Had to avoid eating some foods	46	67	1,48	1,1-2,00
29 Had an unsatisfactory diet	18	42	2,36	1,28-4,35
30 Been unable to eat with dentures	30	50	1,67	1,02-2,72
31 Avoided smiling	38	67	1,76	1,24-2,49
32 Had to interrupt meals	38	55	1,44	1,01-2,06
Psychological Disability				
33 Sleep has been interrupted	38	49	1,29	0,90-1,80
34 Been upset	38	68	1,77	1,26-2,55
35 Found it difficult to relax	37	53	1,45	1,00-2,10
36 Felt depressed	39	58	1,50	1,05-2,12
37 Concentration has been affected	33	48	1,46	1,00-2,18
38 Been embarrassed	35	63	1,82	1,25-2,65
Social Disability				
39 Avoided going out	21	39	1,83	1,06-3,17
40 Been less tolerant of spouse or partner	23	38	1,65	1,03-2,78
41 Had trouble getting on with other people	15	48	3,21	1,67-6,15
42 Been a bit irritable with other people	26	37	1,41	0,9-2,27
43 had difficulty doing usual job	27	36	1,33	0,84-2,1
Handicap				
44 Felt that general health has worsened	20	50	2,49	1,45-4,48
45 Suffered any financial loss	9	38	4,11	1,76-9,6
46 Been unable to enjoy other people's company	16	48	2,95	1,60-5,4
47 Felt that life in general was less satisfying	33	56	1,70	1,14-2,5
48 Been totally unable to function	13	37	1,13	0,75-1,70
49 Been unable to work to full capacity	22	43	1,94	1,16-3,25

Psychological Disability. Significant differences were found in 5 of the 6 questions within this subscale. Upsetting and embarrassment were the problems where HIV-1 positive individuals presented higher impact proportions.

Social Disability: The questions "avoided going out", "been less tolerant of spouse or partner" and "had trouble getting on with other people" revealed significant differences between groups, with the last question exhibiting a proportion of impact in group 2 more than 3 times higher when compared with group 1.

Handicap: This was the subscale where prevalence rates were more elevated in HIV-1 positive patients compared with HIV negative ones. One half of the respondents in group 2 reported that oral health-related problems had affected their general health negatively. Moreover, PR of 1.94 and 2.95 with 95% CI with lower limits above 1 where found for the questions: "Been unable to work to full capacity" and "been unable to enjoy other people's company". The bigger difference between the two groups was related to financial loss, where group 2 exhibited a proportion of impact more than 4 times higher when compared with group 1.

Considering the results from tables I and II which demonstrated significant heterogeneity between the two groups, a stepwise regression model was created to determine the statistically independent correlates of the relationships between OHIP-49 scores (total and subscales) and socio-demographic, clinical and behavioural factors.

The model included all factors which presented statistically significant differences between the two groups namely, gender, age, housing, employment, drug use, HIV status, DMFt, number of decayed teeth, missing teeth, periodontic needs, prosthodontic needs, at least one posterior tooth missing and at least on anterior tooth missing.

Table IV compiles the results of the stepwise regression analysis, displaying the factors that remained included in the model, the cumulative r square, the regression coefficients and its significance. HIV status and DMFt were independently and significantly associated with OHIP scores for total and all subscales. Drug use was independently and significantly associated with OHIP scores for total and all subscales, except for Functional Limitation and Physical Pain, from which it was excluded from the model. Variable "at least one anterior tooth missing" was shown to be significantly and independently associated with total OHIP score, Functional Limitation and Handicap. Housing was associated only with Psychological Disability with a negative regression coefficient, since coding was 0 for "house not owned" and 1 for "house owned", which

generated a smaller impact on the OHRQOL. All other variables were excluded from the model in all subscales and also for total OHIP score.

Table IV. Results of the stepwise regression analysis, displaying the factors that remained included in the model, the cumulative r square, the regression coefficient and its significance

	Final Model	Cumulative r square	Regression coefficient	P
Functional Limitation	DMFt	0,136	0,236	0,001
	HIV Status	0,166	3,816	0,001
	At least 1 anterior tooth missing	0,185	3,014	0,006
Physical Pain	DMFt	0,081	0,254	0,001
	HIV Status	0,096	2,59	0,029
Psychological Discomfort	DMFt	0,130	0,190	0,000
	HIV Status	0,193	3,424	0,000
	Drugs	0,230	2,571	0,000
Physical Disability	DMFt	0,201	0,444	0,000
	HIV Status	0,227	3,420	0,006
	Drugs	0,243	2,625	0,009
Psychological Disability	DMFt	0,084	0,217	0,000
	HIV Status	0,115	3,091	0,001
	Drugs	0,134	2,075	0,018
	Housing	0,146	-2,018	0,036
Social disability	DMFt	0,093	0,170	0,000
	Drugs	0,110	1,854	0,005
	HIV Status	0,112	1,845	0,024
Handicap	DMFt	0,108	0,178	0,010
	HIV Status	0,146	3,711	0,001
	Drugs	0,170	2,747	0,003
	At least 1 anterior tooth missing	0,180	2,177	0,049
OHIPADD score	DMFt	0,161	1,477	0,000
	HIV Status	0,204	21,351	0,000
	Drugs	0,228	12,835	0,010
	At least 1 anterior tooth missing	0,239	9,667	0,036

From the results obtained with the regression model, a generalized univariate analysis was performed for every subscale and for total OHIP score.

Pairwise comparisons with Bonferroni corrections were performed between the two groups. Estimated means were adjusted for all variables which remained in the final regression model, and DMFt was used as a covariate. The results are presented in table V

along with the unadjusted means previously obtained with simple independent t test between groups 1 and 2.

Simple t tests comparing unadjusted means from both groups suggested significant differences in total OHIP score and in all subscales. However and albeit pairwise comparison between groups 1 and 2 estimated means, adjusted for variables with independent effect on the questionnaire scores, demonstrated higher OHIP scores in HIV-1 positive group in every subscale and total OHIP scores, the differences between adjusted means were not significant for Physical Pain, Physical Disability and Social Disability subscales.

Table V. Comparison between unadjusted and adjusted score means for all subscales and total OHIP, standard error of mean and its significance

	VIH-1	Mean	Std. Error Mean	P	Adjusted Mean	Std. Error Mean	P	Adjusting variables
Functional Limitation	NO	13,29	1,16	0,001	15,49	1,03	0,012	DMFt
	YES	*18,82	0,46		*18,56	0,45		At least 1 ATM[1]
Physical Pain	NO	12,61	0,92	0,001	13,73	1,37	0,090	DMFt
	YES	*16,51	0,47		16,23	0,49		
Psychological Discomfort	NO	6,04	0,69	0,001	8,06	0,77	0,001	DMFt
	YES	*11,30	0,34		*11,47	0,32		Drugs
Physical Disability	NO	7,96	1,03	0,001	11,91	1,18	0,121	DMFt
	YES	*14,57	0,55		14,12	0,53		Drugs

Psychological disability	NO	6,04	0,81	0,001	6,92	0,99	0,045	DMFt Drugs Housing
	YES	*10,48	0,41		*10,28	0,40		
Social Disability	NO	3,31	0,60	0,001	5,24	0,37	0,255	DMFt Drugs
	YES	*6,34	0,34		6,21	0,33		
Handicap	NO	3,74	0,67	0,001	6,54	1,10	0,013	DMFt Drugs At least 1 ATM[1]
	YES	*9,65	0,51		*9,82	0,46		
OHIPADD score	NO	52,50	5,25	0,001	67,32	5,67	0,010	DMFt Drugs At least 1 ATM[1]
	YES	*87,45	2,59		*86,16	2,41		

**Statistically significant results*
[1]ATM – Anterior tooth missing

V. DISCUSSION

The results of this study strongly suggest that HIV-1 positive patients present a diminished OHRQOL when compared with non-seropositive patients from the same socio-economic environment. This finding is supported by the higher proportion of positive impacts experienced in group 2 within every question of the OHIP-49, ranging from 37% to 84%. Our results also reveal that variables like HIV positive status, high DMFt index, prostodontic needs and drug use have an independent and negative effect on the OHRQOL, which is in accordance with the hypothesis of this study.

The pre-existing literature on this topic is scarce. The earliest study (Coates *et al*. 1996) assessing the OHRQOL among people living with HIV, conducted in Australia in the 1990´s, administered the same 49-item questionnaire used in the present study. The results obtained have suggested a prevalence of positive impacts about three to eight times higher in the HIV positive group when compared to an age-matched sample of adults from the general population. In our study, there is a clear and significant difference between the two groups regarding the prevalence of positive impacts. However, this difference cannot reach the same proportion. Although it is difficult to compare the results, mainly due to dissimilarities in data collection and reporting (Coates *et al*. reported prevalence estimates for just six individual items in the OHIP) a possible explanation for this small difference in proportion of positive impacts in our study lies in the fact that our HIV negative group is part of the same socio-economic background of the HIV-1 positive group, a disadvantaged population that cannot be compared with the general one.

A 5.5-year prospective cohort study (Mulligan *et al.*, 2008), in which was administered the 14-item OHIP among 92 HIV negative and 597 HIV positive women has also suggested a poorer OHRQOL in the seropositive group. Consistent with the results of the present study, Mulligan *et al*. have found no independent association between HIV viral load and OHIP scores. Jeganathan *et al*. (Jeganathan *et al*., 2011) and Tomar *et al*. (Tomar *et al*., 2011) have reached similar results. According to these studies, clinical variables like CD4 counts and viral load have no influence on the social impact related to oral health.

A recent study (Liberali *et al.*, 2013), which is a repeat of the 1992-1993 study (Coates et al. 1996) to provide additional information in the ART era, has supported the hypothesis that HIV positive patients continue to experience high levels of oral

manifestations and still have significant oral health needs particularly related to the management of periodontal disease. In an opposite way, the results of our study strongly suggest that high DMFt index and prostodontic needs are the major clinical variables that lead to a worst OHRQOL, presenting an independent and negative association with the OHIP scores.

Regarding DMFt index, this study reveals and independent and significant association with OHIP scores for total and all subscales. On average, HIV positive patients present 21.3 decayed, missing or filled teeth, a value almost 2 times higher than the non-seropositive group, which present a DMFt index of 13.3. Although there is no report on dental caries in Portuguese HIV positive population, the last national epidemiological survey conducted in the 1990s (Almeida et al., 1991) have shown that DMFT for 35–44 year-old adults was 10.9, well below the number presented by our HIV positive sample.

According to the results presented in this study, the clinical variable "at least one anterior tooth missing" (prostodontic needs) is significantly and independently associated with total OHIP score, Functional Limitation and Handicap. On the other hand, Locker (Locker, 1992) and Tomar *et al*. (Tomar *et al*., 2011) have suggested denture use to predict a poorer OHRQOL. So, these findings reinforce not only the importance of routine dental prevention measures and early intervention but also the need of an adequate rehabilitation plan.

Our study demonstrates that drug use is a behavioural factor with a negative influence on the OHRQOL, presenting an independent and significant association with OHIP scores for total and all subscales, except for Functional Limitation and Physical Pain. Although intravenous drug use has not been considered a significant risk factor in Mulligan *et al*. study (Mulligan *et al.*, 2008), the national HIV Cost and Services Utilization Study (Coulter *et al*., 2002) has found that intravenous drug users demonstrated the poorest OHRQOL of all HIV exposure groups.

There are some weaknesses in this study. The first is the sample size regarding the control group, which could have been increased. Another limitation is the presence of a significant heterogeneity between the two study groups. However, the results presented are novel an important since this is an analytic study due to the existence of a healthy control group, which allows to test a hypothesis; the study has a robust statistics and the regression analysis produced a reliable model; this is the first study that suggests an independent and negative impact of HIV-1 infection on the OHRQOL of these patients;

studies on this type of population are rare, so this study provides important data that will help to recognize the impact of HIV-1 infection on the OHRQOL.

Our sample is representative of the Portuguese HIV population, therefore the results obtained are likely to be applied. This study provides essential information not only at patient´s level but also at socio-economic level for the oral health community, once it suggests the importance of developing community strategies that help to improve the access of these patients to oral health care, therefore improving their QOL and social integration.

VI. CONCLUSIONS

Within the limitations of this study, it can be concluded that HIV-1 infection has an independent and negative impact on the OHRQOL. Additional factors like a high DMFt index, prostodontic needs and drug use are independently associated with the OHIP scores, therefore presenting a negative effect on the OHRQOL of these patients.

In the current setting, due to the poor oral health and high treatment needs, this population represents an important priority group for prompt delivery of dental care.

Future prospective studies should evaluate the effect of oral rehabilitation on the quality of life of people living with HIV.

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